

Preface

In the early twentieth century following the elucidation of the structure of atoms it became evident that atoms and molecules with even numbers of electrons were far more numerous than those with odd numbers of electrons. In 1916, G. N. Lewis provided the first comprehensive description of ionic and covalent bonds, when he postulated that atoms tend to hold an even number of electrons in their outer shells and a special stability was associated with eight valence electrons, which he speculated were arranged symmetrically at the eight corners of a cube. In 1919, I. Langmuir suggested that the structure of the periodic table could be rationalized using an extension of Lewis' postulates. In 1922, N. Bohr updated his model of the atom by assuming that certain numbers of electrons (for example 2, 8, and 18) corresponded to stable "closed shells." In 1926, Schrödinger established a wave mechanical description of the hydrogen atom which was subsequently extended to polyelectron atoms. Pauli was the first to realize that the complicated numbers of electrons in closed shells can be reduced to the simple rule of *one* per state, if the electron states are defined using four quantum numbers. For this purpose he introduced a new two-valued quantum number, identified by Goudsmit and Uhlenbeck as electron spin. The resulting Pauli Exclusion Principle states that no two electrons in a single atom can have the same four quantum numbers; if n , l , and m_l are the same, m_s must be different such that the electrons have opposite spins.

The idea of shared electron pairs introduced by Lewis provided an effective qualitative picture of covalent bonding and it still forms the basis of the universal notation for chemical communication, but it was Heitler and London who in 1927 developed the first successful quantum mechanical expression for this bonding model. Initially they provided a description of the bonding in molecular hydrogen, but it was subsequently adapted to more complex molecules and its widespread applications were articulated with great conviction by Linus Pauling. An alternative molecular orbital description of chemical bonding originated from Burrau's description of the hydrogen molecule ion and this model was subsequently widely developed by Mulliken and Lennard-Jones. The electrons occupy molecular orbitals which are delocalized over the whole molecule and were filled according to the Aufbau Principle and assigned quantum numbers according to the Pauli

Exclusion Principle. The orbitals are calculated in a self-consistent fashion in a manner analogous to those developed previously for atomic orbitals and are based on linear combination of the atomic orbitals of the individual atoms. The number of molecular orbitals equals the number of atomic orbitals in the atoms being combined to form the molecule. A molecular orbital describes the behavior of one electron in the electric field generated by the nuclei and some average distribution of the other electrons. This approximation proved to be more amenable to computer programming than the valence bond model and was widely developed and used in increasingly less approximate forms from 1960 to 1990.

In the early 1970s, a new electronic structure approach emerged from the physics community and was described as density functional theory (DFT). The total energy of a molecule was expressed as a functional of the total electron density. Hohenburg and Kohn proved the unique relationship between electron density and energy and Kohn and Sham put forward a practical variational DFT approach. Although calculations in solid-state physics had been reported since the 1970s DFT was not considered accurate enough for calculations in quantum chemistry until the 1990s, when the approximations used in the theory were refined to more accurately describe the exchange and correlation interactions. Computational costs for *ab initio* DFT calculations are relatively low when compared to the valence bond and molecular orbital methods. DFT thus began to approach the goals of computational thermochemistry to calculate the energetic properties of chemical processes to an accuracy of 1 kcal mol⁻¹. The widespread acceptance of these methodologies by the chemical community led to Kohn and Pople sharing the Nobel Prize in Chemistry in 1998.

When in 2004 Volumes 112 and 113 of *Structure and Bonding* were devoted to the “Principles and Applications of Density Functional Theory in Inorganic Chemistry” the editors N. Kaltsoyanis and J.E. McGardy noted “It is difficult to overestimate the impact that Density Functional Theory has had on computational quantum chemistry over the last two decades. Indeed, this period has seen it grow from little more than a theoretical curiosity to become a central tool in the computational chemist’s armory.” In these volumes they described recent applications in inorganic and biochemistry and addressed key issues in spectroscopy, mechanistic studies, and magnetism.

As possibly the dominant discipline of the twenty-first century the biological sciences have assimilated analytical, conceptual, and computational techniques from the other natural sciences. The continuing need for interpreting the vast amount of new data from *in vivo* and *in vitro* experiments using causal and deterministic hypothesis requires a wide range of statistical and computational tools and algorithms. As a consequence bioinformatics and mathematical, physical, and chemical biology have flourished and been used to interpret complex natural biological phenomena and pharmaceutical/toxicological effects of chemicals to natural systems.

The universal implications of chemical interactions and more specifically the structure and bonding characteristics of biomolecules suggest that DFT may also play a crucial role *in cerebro* and *in silico* experiments. Establishing the molecular

basis of biological principles by means of quantum mechanical tools has become a realistic possibility given the current accuracy of DFT methods. The present volume opens with an authoritative review of the extensions of DFT (dispersion-corrected functionals, Born–Oppenheimer dynamics, hybrid with molecular mechanics, constrained, and interpretational) from chemical reactions to biochemical systems (containing over a hundred atoms, enzyme kinetics, etc.). The dispersion problem and the development of dispersion-corrected DFT, which may be used accurately to describe weakly bonded biological systems, are further formalized by specific density functional features in the second chapter. Computational models of DFT are used in the next chapter to exemplify the theoretical counterparts of the spectroscopic data to define the binding and activation energies of small molecules with high bioinorganic implications such as water, congeners of molecular oxygen, nitrogen oxides and oxyanions, sulfide, sulfur oxides and oxyanions, carbon dioxide, organic compounds, halogens, molecular hydrogen, and protons. The computational DFT approach as applied to the electronic localization functions and maximum probability domain analyses for modeling metal–porphyrins. These results suggest that the bonding is primarily ionic in porphyrins containing transition and non-transition metals. The last two chapters deal with the important problem of modeling toxicity phenomena using reactivity principles derived from DFT calculations. After introducing the connection between chemical structure and biological information by connecting the chemical reactivity with biological activity within the quantitative structure–activity relationship (QSAR) technique, the possible anticancer activity of two new metal–borane clusters is explored. It is further generalized by the last chapter which describes the full merging of the QSAR with logistic enzyme kinetics. This leads to a description of the mechanisms of chemical–biological interactions in chlorinated-PAHs by means of chemical reactivity principles derived from conceptual DFT.

Overall the volume provides a coherent exposition of the application of DFT to various biological and bioinorganic chemical systems. We hope that it will encourage the DFT community in further refining and extending the electronic models to complex and correlated biological–chemical systems and interactions in the years to come.

We thank the contributors to this volume for the consistent efforts they have made in writing high-class scientific reviews and for providing the readers with a broad perspective which has revealed the widespread uses of DFT in interpreting biological and bioinorganic systems. MVP acknowledges the research and editing facilities provided for the present volume by the Romanian Education and Research Ministry within the project CNCS-UEFISCDI-TE-16/2010-2013. MVP and DMPM sincerely thank the Springer team and in particular Marion Hertel, Ursula Gramm, Elizabeth Hawkins, and Tanja Jaeger for professionally supervising the production of the **Structure and Bonding** series in general and of this volume in particular.

Timișoara, Romania
Oxford, UK

Mihai V. Putz
D. Michael P. Mingos

Applications of Density Functional Theory to Biological
and Bioinorganic Chemistry

Putz, M.V.; Mingos, M.D.P. (Eds.)

2013, XII, 236 p. 107 illus., 41 illus. in color., Hardcover

ISBN: 978-3-642-32749-0